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10/814,555	03/30/2004	Matthew D. Linnik	252312008000	7418

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	
MAIL DATE	**DELIVERY MODE**
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,555	LINNIK ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-19 and 23-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/30/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of August 27, 2007, to the non-final action dated February 26, 2007 has been entered. No claims were cancelled. Claims 1-41 are pending in the application. Claims 1 and 14 have been amended, and claims 27-41 newly added. Claims 7-9 and 20-22 remain withdrawn from consideration, without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claims 1-6, 10-19 and 23-41 are currently under examination.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 3, 5, 6, 16, 18 and 19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite and not further limiting, in the previous office dated February 26, 2007. In view of Applicant's clarification that double stranded DNA epitopes are not limited to nucleotides, as defined by the specification, the previous rejection is hereby withdrawn.

New Claim Rejections - 35 USC § 112- Second Paragraph

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1-6, 10-19, 23-28, 30, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14, 27, 28, 30, 33 and 34 are unclear in the recitation of dosages corresponding to 3mg/kg or higher and 10mg/kg or higher, because the dosages fail to define an upper limit for the dosage to be administered, and thus fail to define the metes and bounds of the claims.

Claims 1 and 14 are further unclear in the recitation of "and wherein **if** the agent is administered in the form of a conjugate of the formula...". Thus, the claims appear incomplete, as

there is no apparent consequence resulting from having administered the agent in the form of a conjugate indicated.

Claims 5-6 and 10-13 depend from claim 1; and claims 15-19 and 23-26 depend from claim 14, and have thus been included in the rejection.

New Claim Rejections - 35 USC § 112- New Matter

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1-6, 10-19 and 23-41 are newly rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art (hereafter the Artisan), that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR §1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claims 1 and 14 are directed to methods of treating SLE and reducing the risk of SLE in an individual, comprising administering to the individual an effective amount of an agent which reduces anti-dsDNA antibody in the individual, and wherein **if** the agent is administered in the form of a conjugate of the formula corresponding to LJP394. It should be noted that LJP-394 is the elected species of agent comprising a dsDNA epitope, under current examination. The instant specification provides a written description support for the claimed therapeutic limitations following administration of LJP394, and not other agents having a different conjugate formula. Therefore, it remains unknown whether agents other than LJP394 have the ability to produce the instantly claimed therapeutic results. Claims 2-6, 10-13, 29-30, 35, 38 and 41 depend from claim 1 and claims 15-19, 23-26, 29-30, 35, 38 and 41 depend from claim 14.

Claims 1, 14, 27, and 28 additionally recite: "administration of the conjugate comprises administering a dose of about 3mg/kg or higher of the conjugate". Claims 30 and 33 recite: "a dose of about 10mg/kg or higher". Claim 32 recites "a dose of about 5mg/kg to about 100mg/kg". Claims 35-37 recite "a dose of about 200mg/kg to about 500mg/kg". Claims 38-40 recite "a dose of about 300 mg". The instant specification is devoid of any such limitation. Applicants state that support for the claims appears *inter alia* at paragraph [0119]. However, no such support is apparent for the limitations, as the preferred range indicated in paragraph [0119]

is "about 150μg to about 5 mg/kg body weight"; with "other dosages, such as about 50 to 100 mg per week, 50 to 250 mg per week, and 50 to 500 mg/week". The instant claims are directed to a dose, that encompasses a single, multiple, repetitive and cumulative dosage. However, the only reference, citing "1μg to about 10 mg/kg body weight or higher every 30 to 60 days, or sooner" is with respect to repetitive administrations (p. 46). In the instant case, claims reciting a dosage of about 3mg/kg or higher, or 10 mg/kg or higher read on embodiments outside the ranges taught by the specification and additionally fail to define an upper limit. Applicants should further note, in the decision in *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of 25%- 60%" and specific examples of "36%" and "50%." A corresponding new claim imitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside the "25% to 60%" range.

Thus, at the time the application was filed, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of the alternative conjugates resulting in a sustained reduction in anti-dsDNA antibody, or the dosages of 3mg/kg or higher and 10mg/kg or higher, as claimed.

MPEP 2163.06 notes: "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure"

This is a new matter rejection.

Response &New Claim Rejections - 35 USC § 112-Scope of Enablement

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1-6, 10-19 and 23-26 stand rejected under 35 U.S.C.§112, first paragraph, because the specification fails to provide an enablement for the full scope of the claimed invention. The rejection set forth on pp. 3-5 of the previous office action dated February 26, 2007 is maintained for claims 1-6, 10-19 and 23-26 and further applied to newly added claims 27-41, for reasons of record.

Applicants traverse this rejection, stating that amendments have been made to claims 1 and 14 that recite administering a dose of about 3 mg/kg or higher of the conjugate, and the sustained reduction of anti-dsDNA antibody for at least about one month. Applicants' arguments have been fully considered, but are not found persuasive.

The amendment of the claims to recite various dosages fail to obviate the grounds for rejection, because the instant specification fails to provide an enablement for a method of treating systemic lupus erythematosus (SLE) and reducing the risk of renal flare in any human individual following the administration of LJP-394, resulting in an indefinitely sustained reduction in anti-dsDNA antibody. Additionally, the newly introduced limitation of sustained reduction of anti-dsDNA antibody for at least about one month, fails to set an upper limit for the duration of antibody reduction and includes an indefinite period of sustained treatment. Moreover, the introduced limitations fail to address the issue of treatment in any human individual, or in any human population following the administration of an effective amount of LJP-394. As the previous office action indicated, the patient population that responded to the treatment regimens with LJP 394 in a statistically significant manner was limited to the sub-population of SLE patients having high affinity antibodies to LJP 394. Further the sustained reduction in antibodies to ds-DNA as depicted in Figures 3 and 4 are limited to the clinical study period and wherein LJP 394 is administered throughout. Furthermore, the phase II/III 90-05 clinical trials summarized in the prior art of Wallace (Exp. Opin. Invest. Drugs 10:111-117; 2001; of record) indicated that the results of the clinical studies may not be extended to all SLE

patients and a sustained reduction in anti-ds-DNA antibodies in a sub-population of SLE patients has not been demonstrated for an indefinite period of time.

Thus it is maintained that the specification is only enabling for a method of treating (SLE) and reducing renal flare in a subpopulation of human individuals characterized by having high affinity IgG antibodies to LJP-394, comprising administering to said individuals an effective amount of LJP-394 to reduce the levels of anti-dsDNA antibodies.

Thus, the rejection is maintained for claims 1-6, 10-19 and 23-26 and further applied to newly added claims 27-41, for reasons of record and the foregoing discussion.

Response & New Claim Rejections - 35 USC § 102

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1-6, 10-19 and 23-26 stand rejected under 35 U.S.C. 102(b) as being anticipated by Wallace (Exp. Opin. Invest. Drugs 10:111-117; 2001). The rejection set forth on pp. 6-7 of the previous office action dated February 26, 2007 is maintained for claims 1-6, 10-19 and 23-26 and further applied to newly added claims 27-41, for reasons of record.

Applicants traverse this rejection and state that in view of the amendments that have been made to claims 1 and 14, to recite a particular dose ("3 mg/kg or higher") is administered if the dsDNA epitope that is administered is in the form of LJP 394, the rejection with the Wallace reference under 35 USC 102(b) is rendered moot. Applicants' arguments have been fully considered, but are not found persuasive.

As indicated above, the instant claims are directed to a dose, that encompasses a single, multiple, repetitive and cumulative dosages. Thus a dose of 3mg/kg may be equivalent to 180 mg for a person of 60 kg in weight. Wallace et al. teach single-dose and multiple-dose administration of 25-200mg of the drug in a phase II study (second paragraph, p. 114), that anticipate the newly introduced limitation. Further, Wallace et al. teach dosages at levels of 100 times the maximum clinical dose in safety and tolerability studies (first column, p. 116). Applicants should further note that as indicated in MPEP 2144.05: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable

ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With respect to Applicants' comment regarding a sustained reduction of anti-dsDNA antibody in the individual as an inherent property of the dose and treatment regimen of SLE patients with LJP 394, it should be noted that the citation of prior art is commensurate with the enabled scope indicated for the instant claims.

Thus, the rejection is maintained for claims 1-6, 10-19 and 23-26 and further applied to newly added claims 27-41, for reasons of record and the foregoing commentary.

Conclusion

Claims 1-6, 10-19 and 23-41 are not allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

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